IN THE CLAIMS

Claims 1-3, 5-9, and 25 to 30 are pending.

Claims 1, 5, 6, 7, 8, 25, 26 and 29 are currently amended.

Claim 4 is cancelled.

Claims 10 to 24 are withdrawn.

Claims 2, 3, 9, 27, 28 and 30 are original.

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WHAT IS CLAIMED IS:

1. [Currently Amended]   A naïve phage display library of antigen-binding fragments cloned derived from llama antibodies derived from a non-immunized llama, said fragments comprising fragments having an antigen-binding affinity with a dissociation constant (K_D) of 5.7×10^{-5} M or lower K_D, each antigen-binding fragment comprising at least a part of the variable heavy domain (V_HH or VH) of a llama antibody.

2. [Original]   A phage display library according to claim 1, wherein the antigen-binding fragment comprises a complete variable heavy domain (V_HH or VH).

3. [Original]   A phage display library according to claim 2, wherein the antigen-binding fragment consist essentially of a variable heavy domain (V_HH or VH) of a llama antibody.

4. [Cancelled] A phage display library according to claim 3, wherein the library is derived from the antibody repertoire of a non-immunized llama.

5. [Currently Amended]   A phage display library according to claim 4, wherein the library is of a size of at least 10^9 clones.

6. [Currently Amended]   A phage display library according to claim 5, wherein the library is of a size of at least 10^8 clones.

7. [Currently Amended]   A phage display library according to claim 4, wherein a the phage vector is a modified fd-tet phage.

8. [Currently Amended]   A phage display library according to claim 7, wherein the library is generated in the absence of a tetracycline.

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9. [Original]   A phage display library according to claim 8, wherein the library is generated as plaques.

10. [Withdrawn]   An antigen-binding fragment derived from a llama antibody, said fragment comprising at least a part of the variable heavy domain (V_HH or VH) of the antibody.

11. [Withdrawn]   An antigen-binding fragment according to claim 10, wherein said fragment comprises a complete variable heavy domain (V_HH or VH) of the antibody.

12. [Withdrawn]   An antigen-binding fragment according to claim 11, wherein said fragment consists essentially of the variable heavy domain (V_HH or VH) of a llama antibody.

13. [Withdrawn]   An antigen-binding fragment according to claim 12, wherein the antibody is selected from the antibody repertoire of a non-immunized lama.

14. [Withdrawn]   An antigen-binding fragment according to claim 13, wherein the complementarity determining regions CDR1/H1, CDR2 and CDR3 of the variable heavy domain (V_HH or VH) are essentially free of cysteine residues.

15. [Withdrawn]   An antigen-binding fragment according to claim 14, wherein the CDR1/H1 region of the variable heavy domain (V_HH or VH) is selected from the group consisting of:

GFTFSSYAMS	(SEQ ID NO: 85)
GFTFSSYYMS	(SEQ ID NO: 86)
GFTFDEHAIG	(SEQ ID NO: 87)
GFTVSSNHMT	(SEQ ID NO: 88)
GFTFSSYHMA	(SEQ ID NO: 89)
GFTFSRHQMS	(SEQ ID NO: 91)

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GFTFRTYYMN (SEQ ID NO: 92)

GFIFSSYAMS (SEQ ID NO: 93)

GFTFSTYAMT (SEQ ID NO: 95)

GFTFSGYAMS (SEQ ID NO: 99)

GFAFSNYRMT (SEQ ID NO: 100)

GFTFSRYAMS (SEQ ID NO: 101)

16. [Withdrawn] An antigen-binding fragment according to claim 14, wherein the CDR2 region of the variable heavy domain (V_HH or VH) is selected from the group consisting of:

GIEGGGGITRYADSVKG (SEQ ID NO: 102)

TIKPGGGSTYYADSVKG (SEQ ID NO: 103)

TIDIGGGRTYADSVKG (SEQ ID NO: 104)

RISSDGRNTYYADSVKG (SEQ ID NO: 105)

TINPGDGSTYYADSVKG (SEQ ID NO: 106)

HIDTGGSTWYAASVKG (SEQ ID NO: 107)

TINIDGSSTYYADSVRG (SEQ ID NO: 109)

GINSFGGSKYYADSVKG (SEQ ID NO: 110)

TINTSGRGTYYADSVKG (SEQ ID NO: 112)

AINSGGGSTSYADSVKG (SEQ ID NO: 113)

HIDTGGGSTWYAASVKG (SEQ ID NO: 114)

DINSGGDSTRNADSVKG (SEQ ID NO: 115)

SINSGGGSTYYADSVKG (SEQ ID NO: 116)

RINSIGDRISYADSVKG (SEQ ID NO: 117)

17. [Withdrawn] An antigen-binding fragment according to claim 14, wherein the CDR3 region of the variable heavy domain (V_HH or VH) is selected from the group consisting of:

AHGGYGAFGS (SEQ ID NO: 119)

YSGGALDA (SEQ ID NO: 122)

LSQGAMDY (SEQ ID NO: 124)

IDRERAFTS (SEQ ID NO: 127)

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IDWERAFTS	(SEQ ID NO: 128)
QGYAGSYDY	(SEQ ID NO: 129)
LGVPGTFDY	(SEQ ID NO: 130)
TNRGIFDY	(SEQ ID NO: 131)
TPGSSGVYEY	(SEQ ID NO: 132)
TQTGSHDY	(SEQ ID NO: 133)
QVGTAYDY	(SEQ ID NO: 134)
RRGSSGVYEY	(SEQ ID NO: 135)

18. [Withdrawn]   An antigen-binding fragment according to claim 14, wherein said fragment has at position 45 a residue of an amino acid other than cysteine.

19. [Withdrawn]   An antigen-binding fragment according to claim 18, wherein amino acid residues of the VL interface of the variable heavy domain (V$_H$H or VH) are Gly at position 44, Leu, Phe, Pro, or Arg at position 45, and Trp, Tyr, or Phe at position 47.

20. [Withdrawn]   An antigen-binding fragment according to claim 19, wherein amino acid residues at positions 44, 45 and 47 are Gly, Leu and Trp, respectively.

21. [Withdrawn]   An antigen-binding fragment according to claim 19, wherein amino acid residues at positions 44, 45 and 47 are Gly, Pro and Trp, respectively.

22. [Withdrawn]   An antigen-binding fragment according to claim 18, wherein amino acid residues of the VL interface of the variable heavy domain (V$_H$H or VH) are Glu at position 44, Arg at position 45, and Phe, Ile, Val, or Gly at position 47.

23. [Withdrawn]   An antigen-binding fragment according to claim 18, wherein amino acid residues of the VL interface of the variable heavy domain

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(V$_H$H or VH) are Gln, Gly, Lys, Ala, or Asp at position 44, Arg at position 45, and Leu, Phe, or Trp at position 47.

24. [Withdrawn]   An antigen-binding fragment according to claim 18, wherein amino acid residues at positions 6, 23, 74, 82a, 83, 84, 93 and 108 are Ala, Ala, Ala, Asn, Lys, Pro, Ala and Gln, respectively.

25. [Currently Amended]   A camelid cDNA library comprising nucleotide sequences coding for antigen-binding fragments of conventional heavy chain llama antibodies, said library obtained by performing the steps of:

    (a) isolating lymphocytes from a biological sample obtained from a non-immunized llama;

    (b) isolating total RNA from the lymphocytes;

    (c) reverse-transcribing the RNA and amplifying the cDNA RNA sequences coding for the antigen-binding fragments;

    (d) cloning the amplified cDNA in a vector, and

    (e) recovering the obtained clones.

26. [Original] A cDNA library according to claim 25, wherein each antigen-binding fragment comprises at least a part of the variable heavy domain (V$_H$H or VH) of the antibody.

27. [Original] A cDNA library according to claim 26, wherein the antigen-binding fragment comprises a complete variable heavy domain (V$_H$H or VH) of the antibody.

28. [Original] A cDNA library according to claim 27, wherein the antigen-binding fragment consists essentially of the variable heavy domain (V$_H$H or VH) of a llama heavy chain antibody.

29. [Currently Amended]   A cDNA library according to claim 28, wherein a the vector employed therein is a filamentous bacteriophage.

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30. [Original] A cDNA library according to claim 29, wherein the filamentous bacteriophage is fd-tet phage.

31. [Withdrawn]   A process for the preparation of an antigen-binding fragment of a llama antibody, said fragment binding to a predetermined antigen, said process comprising the steps of:

    (a) isolating lymphocytes from a biological sample obtained from a non-immunized llama;

    (b) isolating total RNA from the lymphocytes;

    (c) reverse-transcribing and amplifying RNA sequences coding for antigen-binding fragments;

    (d) cloning the cDNA sequences so obtained into a cloning vector, said first vector capable of a surface display of the corresponding antigen-binding fragments;

    (e) subjecting the clones to antigen affinity selection and recovering clones having the desired affinity;

    (f) for the recovered clones, amplifying DNA sequences coding for antigen-binding fragments;

    (g) cloning the amplified DNA sequences into an expression vector;

    (h) transforming host cells with the expression vector under conditions allowing expression of DNA coding for antigen binding fragments; and

    (i) recovering the antibody fragments having the desired specificity.

32. [Withdrawn]   A process according to claim 31, wherein the antigen-binding fragment comprises at least a part of the variable heavy domain ($V_H H$ or VH) of the llama antibody.

33. [Withdrawn]   A process according to claim 32, wherein the antigen-binding fragment comprises a complete variable heavy domain ($V_H H$ or VH) of the llama antibody.

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34. [Withdrawn] A process according to claim 33, wherein the antigen-binding fragment consists essentially of the variable heavy domain (V_HH or VH) of a llama antibody.

35. [Withdrawn] A process according to claim 34, wherein the cloning vector is selected from the group consisting of bacteriophages, bacteria, and yeasts.

36. [Withdrawn] A process according to claim 35, wherein the cloning vector is a filamentous bacteriophage.

37. [Withdrawn] A process according to claim 36, wherein the filamentous bacteriophage is fd-tet phage.

38. [Withdrawn] A process according to claim 31, wherein the expression vector is a plasmid, a phage, a virus, a YAC, or a cosmid.

39. [Withdrawn] A process according to claim 31, wherein the host cells are prokaryotic cells or eukaryotic cells.

40. [Withdrawn] A process according to claim 39, wherein the eukaryotic cells are selected from the group consisting of yeast cells, mammalian cells, plant cells and protozoan cells.

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